

## Renal Effect of Low-Dose Dopamine in High-Risk Patients Undergoing Coronary Angiography

Gare et al. (1) report no advantage of dopamine over “adequate hydration” in patients with mild to moderate renal insufficiency undergoing coronary angiography. The absence of a clinically important effect is no surprise, for dopamine (2 mg/kg/min) would not be a sufficient vasodilator to counteract such a potent renal afferent arteriole vasoconstrictor as intrarenal adenosine. The kidney responds to contrast media-induced osmotic stress with afferent arteriolar vasoconstriction. This tubuloglomerular feedback response is largely mediated by adenosine, a mechanism that has been confirmed by both animal and clinical studies (2–5). In our randomized and blinded studies, the magnitude of adenosine release and depression of creatinine clearance was proportional to the osmolality of the contrast agent, essentially a dose-response relation (2). It is attenuated by the adenosine receptor blocker theophylline (3–5).

When pretreated with long-acting theophylline in addition to hydration with D5W or half-normal saline, patients with moderate renal dysfunction (creatinine  $\leq 2.0$  mg/dl) are reliably protected from the nephrotoxic effects of contrast media (3–5). We currently prescribe Theodur (3 mg/kg) orally the night before and b.i.d. the day of angiography. It is critical that theophylline be administered before contrast injection, but prolonged treatment after angiography is unnecessary.

Theophylline prophylaxis to attenuate contrast-media nephrotoxicity has not been adopted by cardiologists, perhaps because the studies appeared in journals they do not normally read. Theophylline prophylaxis is effective, safe, and inexpensive. In view of the magnitude of the clinical problem of contrast-media nephrotoxicity, we wish to bring this therapeutic strategy to the attention of the readers of *JACC*.

**Richard E. Katholi, MD, FACC**  
**George J. Taylor, MD, FACC**  
Cardiovascular Consultants, Ltd.  
Springfield, Illinois

PII S0735-1097(00)00666-5

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## REPLY

Thank you for your interest in our article on the renal effect of low-dose dopamine in high-risk patients undergoing coronary

angiography (1). We found no important renal protective effect of dopamine in patients at high risk for contrast nephropathy (CN) undergoing coronary angiography. We agree that the vasodilator effect of low-dose dopamine may be too small to counteract the afferent arteriolar vasoconstriction induced by the contrast medium. Higher doses of dopamine, however, may contribute to even more severe vasoconstriction.

We have also been interested in the adenosine receptor blocking effect of theophylline. We found that the acute renal failure induced by indomethacin and contrast medium in rats with diabetes mellitus (DM) was mediated by adenosine via suppression of renal and/or systemic  $\text{NO}_2^-/\text{NO}_3^-$  production and that theophylline reversed  $\text{NO}_2^-/\text{NO}_3^-$  secretion to levels similar to those of DM rats (2). The role of theophylline as a means of reducing CN in the clinical setting, however, is not well defined. Although Katholi (3) and Kolonko (4) have found some beneficial effect of theophylline, more recent studies focusing on higher-risk patients failed to demonstrate such effect. Abizaid et al. (5) found that neither aminophylline nor dopamine reduced the incidence of CN compared with saline hydration alone, in patients with serum creatinine  $\geq 1.5$  mg/dl. Erley et al. (whose previous study was cited by Katholi and Taylor in their present Letter to the Editor) randomized 80 patients with serum creatinine  $\geq 1.5$  mg/dl to either 810 mg of theophylline daily or placebo (6). They found that hydration alone was sufficient to preserve glomerular filtration and that theophylline had no additional benefit; they suggested that theophylline might be beneficial in patients for whom sufficient hydration is difficult, such as patients with severe congestive heart failure (6). Such patients, however, are usually treated with multiple medications, and adding theophylline at a sufficient dose may be accompanied by intolerable side effects.

Therefore, it seems to us that the advantages of theophylline in reducing the detrimental effect of contrast media, especially in high-risk patients, have yet to be proven. The prevention of CN in patients receiving contrast media should be based, at the present time, on adequate hydration accompanied by diuresis when needed.

**Morris Mosseri, MD**

**Meir Gare, MD**

**Devorah Rubinger, MD**

Prairie Cardiology Department

Hadassah Hebrew University Medical Center

Jerusalem, Israel

PII S0735-1097(00)00665-3

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